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L8	antiviral	15308	L8
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L6	edn or eosinophil-derived near3 neurotoxin	3202	L6
L5	l1 and l2 and l3 and l4	9	L5
L4	hiv near6 rev near4 bind$	132	L4
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L2	splice adj donor	2481	L2
L1	hiv near5 packag$	233	L1

END OF SEARCH HISTORY

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Search Results - Record(s) 1 through 4 of 4 returned.

☐ 1. 20020102604 . 07 Dec 00. 01 Aug 02. Full-length human cDNAs encoding potentially secreted proteins. Milne Edwards, Jean-Baptiste Dumas, et al. 435/7.1; 530/350 536/23.1 G01N033/53 C07H021/02 C07H021/04 C07K001/00 C07K014/00 C07K017/00.

☐ 2. 20020006961 . 01 May 01. 17 Jan 02. Method and composition for treating mammalian nasal and sinus diseases caused by inflammatory response. Katz, Stanley E., et al. 514/625; 514/557 A61K031/19 A61K031/16.

☐ 3. 6426070 . 09 May 00; 30 Jul 02. Methods for inactivating enveloped RNA virus particles and compositions for use therewith. Rosenberg; Helene F., et al. 424/94.61; 424/185.1 424/211.1 435/238 435/69.2 530/350 530/380. A61K038/47 A61K039/155 A61K035/14 A61K038/16 G01N033/86.

☐ 4. 6395276 . 01 May 98; 28 May 02. Immunotoxins directed against malignant cells. Rybak; Susanna M., et al. 424/179.1; 424/134.1 424/141.1 424/178.1 424/183.1 424/192.1 424/193.1 514/12 514/44 530/387.3 530/391.7. A61K039/395 A61K038/00 A61K039/385 A61K039/00 C12P021/08.

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Terms	Documents
17 and 18	4

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Search Results - Record(s) 1 through 9 of 9 returned.

☐ 1. 20010031257 . 15 Sep 95. 18 Oct 01. RECOMBINANT FOAMY VIRUS VECTORS FOR MEDICINAL AND DIAGNOSTIC USES, AND PROCESSES FOR PREPARING RECOMBINANT FOAMY VIRUS VECTORS. MEULEN, VOLKER T., et al. 424/93.21; 435/320.1 514/44 536/23.1 A61K048/00 C07H021/04 C12N015/86.

☐ 2. 20010007767 . 25 Nov 97. 12 Jul 01. NOVEL PROPERTY EFFECTING AND/OR PROPERTY EXHIBITING COMPOSITIONS FOR THERAPEUTIC AND DIAGNOSTIC USES. RABBANI, ELAZAR, et al. 435/320.1; 435/243 435/325 435/6 435/91.1 435/91.4 514/44 536/23.1 536/24.1 536/24.5 C07H021/04 C12Q001/68 A61K048/00 C12N015/00 C12N005/02 C12N005/00 C12N001/00 C07H021/02.

☐ 3. 20010006816 . 25 Nov 97. 05 Jul 01. NOVEL PROPERTY EFFECTING AND/OR PROPERTY EXHIBITING COMPOSITIONS FOR THERAPEUTIC AND DIAGNOSTIC USES. RABBANI, ELAZAR, et al. 435/440; 435/320.1 435/325 435/442 435/455 435/91.1 514/44 536/23.1 536/24.3 536/24.5 C07H021/04 C12Q001/68 C12N015/00 A61K031/70 A01N043/04 C12N015/85 C07H021/02.

☐ 4. 20010006815 . 25 Nov 97. 05 Jul 01. NOVEL PROPERTY EFFECTING AND/OR PROPERTY EXHIBITING COMPOSITIONS FOR THERAPEUTIC AND DIAGNOSTIC USES. RABBANI, ELAZAR, et al. 435/440; 435/320.1 435/325 435/442 435/455 435/91.1 514/44 536/23.1 536/24.3 536/24.5 C12N015/09 C12Q001/68 C07H021/04 C12N015/85 C12N015/00.

☐ 5. 20010006814 . 25 Nov 97. 05 Jul 01. NOVEL PROPERTY EFFECTING AND/ OR PROPERTY EXHIBITING COMPOSITIONS FOR THERAPEUTIC AND DIAGNOSTIC USES. RABBANI, ELAZAR, et al. 435/440; 435/243 435/252.3 435/320.1 435/325 435/442 435/455 435/91.1 536/23.1 536/24.3 536/24.5 C07H021/04 C12Q001/68 C12N015/01 C12N015/00 C12N015/70 C12N005/02 C12N005/00 C12N015/09 A61K048/00 C07H021/02.

☐ 6. 6303295 . 12 Jul 96; 16 Oct 01. Selenoproteins, coding sequences and methods. Taylor; Ethan Will, et al. 435/6; 530/350 530/400 536/23.1 536/23.74. C12Q001/68.

☐ 7. 6153382 . 15 Sep 97; 28 Nov 00. Viral growth inhibition. Karn; Jonathan, et al. 435/6; 514/44 536/24.1. C12Q001/68.

☐ 8. 5786145 . 10 Oct 95; 28 Jul 98. Oligonucleotide competitors for binding of HIV RRE to REV protein and assays for screening inhibitors of this binding. Karn; Jonathan, et al. 435/6; 514/44 536/24.1. C07H021/02 C12Q001/68.

☐ 9. 5646032 . 28 Nov 94; 08 Jul 97. Recombinant foamy virus vectors for medicinal, and diagnostic uses, and processes for preparing recombinant foamy virus vectors. ter Meulen; Volker, et al. 435/325; 435/320.1 435/350 435/352 435/357 435/358 435/364 435/366 435/372. C12N005/16 C12N015/86.

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     (FILE 'HOME' ENTERED AT 18:25:02 ON 14 JAN 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 18:25:23 ON 14 JAN
     2003
L1             8 S HIV(5A)PACKAGING(W)SITE
L2           447 S HIV(5A)PACKAGING
L3        432474 S SPLICE(W)DONOR OR SD
L4         62852 S SPLICE(W)ACCEPTOR OR SA
L5           484 S HIV(6A)REV(4A)BIND?
L6             0 S L2 AND L3 AND L4 AND L5
L7             1 S L2 AND L3 AND L4

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L7   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
AN   1999:764177  CAPLUS
DN   132:19626
TI   Efficient gene delivery by multiply attenuated HIV-1-based lentiviral
     transducing vectors that show efficient packaging
IN   Chang, Lung-Ji; Cui, Yan; Iwakuma, Tomoo
PA   University of Florida, USA
SO   PCT Int. Appl., 197 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 5
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   WO 9961598         A2    19991202       WO 1999-US11634  19990526
     WO 9961598         A3    20000413
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
             KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
             MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
             TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9942078         A1    19991213       AU 1999-42078    19990526
PRAI US 1998-86635P     P     19980526
     WO 1999-US11634    W     19990526
AB   A method of constructing HIV-1-based lentiviral transducing vectors with
     increased packaging efficiency and minimal recombination potentials for
     target gene delivery in gene therapy was described.  The parental
     packaging vector pHP-1 contained a modified 5' HIV-1 LTR, a novel major
     splice donor site derived from RSV, the entire gag-,
     pol-env, vif, vpr, vpu, tat, rev genes, and a selectable gpt marker gene,
     and an SV40 polyadenylation signal and multiple derivs. were generated by
     deletion and mutation.  Deletion in the env, and in the 5' LTR, of vpr,
     vif, and vpu in these derivs. packaging vectors did not affect the
     packaging efficiency and these viral particles showed similar protein
     level and even higher titers compared to the wild type HIV-1 expressing
     vector.  However, tat-minus derivs. are deficient in GAG-POL processing
     and can be complemented by cotransfecting the packaging cell lines with a
     tetracycline-inducible construct expressing HIV-1 tat.  Two families of
     transducing vectors were constructed with pTV.phi. using synthetic
     packaging signals and pTV.DELTA. using deleted HIV-1
     packaging signals in which pTV.phi. were packaged much less
     efficiently than pTV.DELTA..  These packaging and transducing vectors
     efficiently transduced actively dividing including rhabdomyosarcoma cell
     TE671, kidney carcinoma cell 293T, hepatoma cell HepG2 and Hela cells.
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They also efficiently transduced non-dividing and terminally differentiated cells including mitomycin C-treated TE671 cell and Hela cell, CD34+ human hematopoietic stem cell (HSC), primary neurons, monocyte-derived macrophages and mouse leg muscles by i.m. injection. The protocol for HSC transduction were optimized by coculturing target cells with retroviral producer cells, treating target cells with mitomycin C and cotransfecting the target cells with constructs expressing growth factor such as human IL-3, or G-CSF, or flt3 ligand. HIV-1 essential elements U3, **SD**, gag AUG, gag-pol, env, tat, rev, and 3' **SA** sites and all the necessary genes in transducing vectors were also deletable to minimize the recombination potential and improve the safety of gene therapy. The primary packaging signal were narrowed down into the sequences of SL2 and SL4 by further reducing the overlapped sequences between transducing vectors and the packaging vectors. The effective gene delivery using these lentiviral vectors has a great potential in human gene therapy.

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     (FILE 'HOME' ENTERED AT 18:25:02 ON 14 JAN 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 18:25:23 ON 14 JAN
     2003
L1             8 S HIV(5A)PACKAGING(W)SITE
L2           447 S HIV(5A)PACKAGING
L3        432474 S SPLICE(W)DONOR OR SD
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L5           484 S HIV(6A)REV(4A)BIND?
L6             0 S L2 AND L3 AND L4 AND L5
L7             1 S L2 AND L3 AND L4
L8         10670 S EDN OR EOSINOPHIL-DERIV?(3A)NEUROTOXIN OR RNASE(W)A
L9           388 S (NUCLEIC(W)ACID OR POLYNUCLEOTIDE OR DNA)(8A)L8
L10          261 S (NUCLEIC(W)ACID OR POLYNUCLEOTIDE OR DNA)(5A)L8
L11          219 S (SUPPRESS? OR INHIBIT? OR DIMINISH? OR DECREAS?)(6A)REPLICATI
L12            0 S L10(S)L11
L13            0 S L10 AND L11
L14          161 DUP REM L10 (100 DUPLICATES REMOVED)
L15          166 S (NUCLEIC(W)ACID OR POLYNUCLEOTIDE OR DNA)(3A)L8
L16          107 DUP REM L15 (59 DUPLICATES REMOVED)

=> d au ti so 30-69 l16

L16  ANSWER 30 OF 107     MEDLINE                        DUPLICATE 10
AU   Heinze B
TI   RAPD reactions from crude plant DNA. Adding RNase
     A as a "helper enzyme".
SO   MOLECULAR BIOTECHNOLOGY, (1994 Jun) 1 (3) 307-10.
     Journal code: 9423533. ISSN: 1073-6085.

L16  ANSWER 31 OF 107     MEDLINE                        DUPLICATE 11
AU   Wang Q; Orrison B M; Marini J C
TI   Two additional cases of osteogenesis imperfecta with substitutions for
     glycine in the alpha 2(I) collagen chain. A regional model relating
     mutation location with phenotype.
SO   JOURNAL OF BIOLOGICAL CHEMISTRY, (1993 Nov 25) 268 (33) 25162-7.
     Journal code: 2985121R. ISSN: 0021-9258.

L16  ANSWER 32 OF 107  CAPLUS  COPYRIGHT 2003 ACS
AU   Clemmesen, Catriona
TI   Improvements in the fluorometric determination of the RNA and DNA content
     of individual marine fish larvae
SO   Marine Ecology:  Progress Series (1993), 100(1-2), 177-83
     CODEN: MESEDT; ISSN: 0171-8630

L16  ANSWER 33 OF 107  CAPLUS  COPYRIGHT 2003 ACS
AU   Rees, William A.; Yager, Thomas D.; Korte, John; Von Hippel, Peter H.
TI   Betaine can eliminate the base pair composition dependence of DNA melting
SO   Biochemistry (1993), 32(1), 137-44
     CODEN: BICHAW; ISSN: 0006-2960

L16  ANSWER 34 OF 107  CAPLUS  COPYRIGHT 2003 ACS
AU   Birdsall, David L.; McPherson, Alexander
TI   Crystal structure disposition of thymidylic acid tetramer in complex with
     ribonuclease A
SO   Journal of Biological Chemistry (1992), 267(31), 22230-6
     CODEN: JBCHA3; ISSN: 0021-9258

L16  ANSWER 35 OF 107     MEDLINE                        DUPLICATE 12
AU   Miyata S; Ohshima A; Inouye S; Inouye M
TI   In vivo production of a stable single-stranded cDNA in Saccharomyces
```

cerevisiae by means of a bacterial retron.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1992 Jul 1) 89 (13) 5735-9.
Journal code: 7505876. ISSN: 0027-8424.

L16 ANSWER 36 OF 107 MEDLINE DUPLICATE 13
AU Fajkus J; Reich J
TI Stable DNA-polypeptide complexes from eukaryotic nuclei purified on heparin Sepharose.
SO FOLIA BIOLOGICA, (1992) 38 (5) 307-15.
Journal code: 0234640. ISSN: 0015-5500.

L16 ANSWER 37 OF 107 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. DUPLICATE 14
AU Tremblay, Stephane D.; Gugg, Siegfried; Lafontaine, Jean G. (1)
TI Ultrastructural, cytochemical and immunocytochemical investigation of the interphase nucleus in the unicellular green alga Chlamydomonas reinhardtii.
SO Biology of the Cell (Paris), (1992) Vol. 76, No. 1, pp. 73-86.
ISSN: 0248-4900.

L16 ANSWER 38 OF 107 CAPLUS COPYRIGHT 2003 ACS
AU Iwahana, Hiroyuki
TI RNase A cleavage analysis
SO Taisha (1991), 28(9), 713-20
CODEN: TSHAAW; ISSN: 0372-1566

L16 ANSWER 39 OF 107 MEDLINE DUPLICATE 15
AU Gagna C E; Mitchell O G; Chen J H
TI Fixation and immunolocalization of left-handed Z-DNA sequences in the calf lens.
SO LENS AND EYE TOXICITY RESEARCH, (1991) 8 (4) 489-509.
Journal code: 8916639. ISSN: 1042-6922.

L16 ANSWER 40 OF 107 CAPLUS COPYRIGHT 2003 ACS
AU Brown, T. A.
TI Recipes and general procedures
SO Essent. Mol. Biol. (1991), Volume 2, 256-9. Editor(s): Brown, Terence A. Publisher: IRL, Oxford, UK.
CODEN: 59FGAZ

L16 ANSWER 41 OF 107 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AU HAMANN K J; BARKER R L; TEN R M; GLEICH G J
TI THE MOLECULAR BIOLOGY OF EOSINOPHIL GRANULE PROTEINS.
SO 18TH SYMPOSIUM OF THE COLLEGIUM INTERNATIONALE ALLERGOLOGICUM ON CELLULAR AND MOLECULAR NETWORKS IN CLINICAL IMMUNOLOGY AND ALLERGY, FUNCHAL, MADEIRA, NORTH ATLANTIC OCEAN, SEPTEMBER 22-26, 1990. INT ARCH ALLERGY APPL IMMUNOL. (1991) 94 (1-4), 202-209.
CODEN: IAAAAM. ISSN: 0020-5915.

L16 ANSWER 42 OF 107 CAPLUS COPYRIGHT 2003 ACS
AU Hawkins, J. Ross; Dalgleish, Raymond
TI The detection and mapping of point mutations by RNase A cleavage
SO Methods in Molecular Biology (Totowa, NJ, United States) (1991), 9(Protoc. Hum. Mol. Genet.), 111-21
CODEN: MMBIED; ISSN: 1064-3745

L16 ANSWER 43 OF 107 CAPLUS COPYRIGHT 2003 ACS
AU Bentley, David R.; Roberts, Roland G.; Montandon, Jane
TI Rapid methods for detection of polymorphic markers in genomic DNA
SO Methods in Molecular Biology (Totowa, NJ, United States) (1991), 9(Protoc. Hum. Mol. Genet.), 51-68
CODEN: MMBIED; ISSN: 1064-3745

L16 ANSWER 44 OF 107 MEDLINE DUPLICATE 16
AU Gagna C E; Chen J H; Lavers G C; Mitchell O G; Zheng S H; Chen L C
TI The presence of Z-helical conformation in DNA of the calf lens.
SO LENS AND EYE TOXICITY RESEARCH, (1991) 8 (1) 27-42.
Journal code: 8916639. ISSN: 1042-6922.

L16 ANSWER 45 OF 107 MEDLINE DUPLICATE 17
AU Witmer M R; Falcomer C M; Weiner M P; Kay M S; Begley T P; Ganem B; Scheraga H A
TI U-3'-BCIP: a chromogenic substrate for the detection of **RNase A** in recombinant **DNA** expression systems.
SO NUCLEIC ACIDS RESEARCH, (1991 Jan 11) 19 (1) 1-4.
Journal code: 0411011. ISSN: 0305-1048.

L16 ANSWER 46 OF 107 MEDLINE DUPLICATE 18
AU Shibata D; Almoguera C; Forrester K; Dunitz J; Martin S E; Cosgrove M M; Perucho M; Arnheim N
TI Detection of c-K-ras mutations in fine needle aspirates from human pancreatic adenocarcinomas.
SO CANCER RESEARCH, (1990 Feb 15) 50 (4) 1279-83.
Journal code: 2984705R. ISSN: 0008-5472.

L16 ANSWER 47 OF 107 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AU KAUFMAN D L; RAMESH V; MCCLATCHEY A I; MENKES J H; TOBIN A J
TI DETECTION OF POINT MUTATIONS ASSOCIATED WITH GENETIC DISEASES BY AN EXON SCANNING TECHNIQUE.
SO GENOMICS, (1990) 8 (4), 656-663.
CODEN: GNMCEP. ISSN: 0888-7543.

L16 ANSWER 48 OF 107 MEDLINE DUPLICATE 19
AU Theophilus B D; Latham T; Grabowski G A; Smith F I
TI Comparison of RNase A, a chemical cleavage and GC-clamped denaturing gradient gel electrophoresis for the detection of mutations in exon 9 of the human acid beta-glucosidase gene.
SO NUCLEIC ACIDS RESEARCH, (1989 Oct 11) 17 (19) 7707-22.
Journal code: 0411011. ISSN: 0305-1048.

L16 ANSWER 49 OF 107 MEDLINE DUPLICATE 20
AU Oglesbee M; Tatalick L; Rice J; Krakowka S
TI Isolation and characterization of canine distemper virus nucleocapsid variants.
SO JOURNAL OF GENERAL VIROLOGY, (1989 Sep) 70 (Pt 9) 2409-19.
Journal code: 0077340. ISSN: 0022-1317.

L16 ANSWER 50 OF 107 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AU HAMANN K; BARKER R; LOEGERING D; PEASE L; GLEICH G
TI NUCLEOTIDE SEQUENCE OF HUMAN **EOSINOPHIL-DERIVED NEUROTOXIN EDN** COMPLEMENTARY **DNA** IDENTITY OF DEDUCED AMINO ACID SEQUENCE WITH THAT OF HUMAN URINARY NONSECRETORY RNASE.
SO 73RD ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, NEW ORLEANS, LOUISIANA, USA, MARCH 19-23, 1989.
FASEB (FED AM SOC EXP BIOL) J. (1989) 3 (4), A1334.
CODEN: FAJOEC. ISSN: 0892-6638.

L16 ANSWER 51 OF 107 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AU BARKER R L; LOEGERING D A; TEN R; HAMANN K J; PEASE L R; GLEICH G J
TI HUMAN EOSINOPHIL CATIONIC PROTEIN ECP COMPLEMENTARY **DNA** HOMOLOGY WITH HUMAN **EOSINOPHIL-DERIVED NEUROTOXIN** EDN AND OTHER RNASES.
SO 73RD ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, NEW ORLEANS, LOUISIANA, USA, MARCH 19-23, 1989.
FASEB (FED AM SOC EXP BIOL) J. (1989) 3 (4), A1333.
CODEN: FAJOEC. ISSN: 0892-6638.

L16 ANSWER 52 OF 107 CAPLUS COPYRIGHT 2003 ACS
AU Abe, T.; Takahashi, H.; Holmes, M. D.; Curiel, D. T.; Crystal, Ronald G.
TI Ribonuclease A cleavage combined with the polymerase chain reaction for detection of the Z mutation of the alpha-1-antitrypsin gene
SO American Journal of Respiratory Cell and Molecular Biology (1989), 1(4), 329-34
CODEN: AJRBEL; ISSN: 1044-1549

L16 ANSWER 53 OF 107 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AU ABE T; TAKAHASHI H; HOLMES M; CURIEL D; CRYSTAL R G
TI RNASE CLEAVAGE COMBINED WITH THE POLYMERASE CHAIN REACTION FOR DETECTION OF THE Z MUTATION OF THE ALPHA-1 ANTITRYPSIN GENE.
SO ANNUAL MEETING OF THE AMERICAN LUNG ASSOCIATION AND THE AMERICAN THORACIC SOCIETY, CINCINNATI, OHIO, USA, MAY 14-17, 1989. AM REV RESPIR DIS. (1989) 139 (4 PART 2), A202.
CODEN: ARDSBL. ISSN: 0003-0805.

L16 ANSWER 54 OF 107 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AU WEINER M P; SCHERAGA H A
TI A SET OF MACINTOSH COMPUTER PROGRAMS FOR THE DESIGN AND ANALYSIS OF SYNTHETIC GENES.
SO COMPUT APPL BIOSCI, (1989) 5 (3), 191-198.
CODEN: COABER. ISSN: 0266-7061.

L16 ANSWER 55 OF 107 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AU HAMANN K J; BARKER R L; LOEGERING D A; PEASE L R; GLEICH G J
TI SEQUENCE OF HUMAN **EOSINOPHIL-DERIVED NEUROTOXIN** COMPLEMENTARY **DNA** IDENTITY OF DEDUCED AMINO ACID SEQUENCE WITH HUMAN NONSECRETORY RNASES.
SO GENE (AMST), (1989) 83 (1), 161-168.
CODEN: GENED6. ISSN: 0378-1119.

L16 ANSWER 56 OF 107 MEDLINE DUPLICATE 21
AU Choder M; Aloni Y
TI RNA polymerase II allows unwinding and rewinding of the DNA and thus maintains a constant length of the transcription bubble.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1988 Sep 15) 263 (26) 12994-3002.
Journal code: 2985121R. ISSN: 0021-9258.

L16 ANSWER 57 OF 107 MEDLINE DUPLICATE 22
AU Cassani G
TI Influence of the cellular host-vector system on the quality of therapeutic proteins obtained by recombinant DNA technology.
SO ARZNEIMITTEL-FORSCHUNG, (1988 May) 38 (5) 762-4.
Journal code: 0372660. ISSN: 0004-4172.

L16 ANSWER 58 OF 107 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AU ATWEH G F; BASERGA S J; BRICKNER H E
TI A NEW METHOD FOR DETECTING SINGLE BASE MUTATIONS IN MESSENGER RNA.
SO FORTY-FIFTH ANNUAL NATIONAL MEETING OF THE AMERICAN FEDERATION FOR CLINICAL RESEARCH, WASHINGTON, D.C., USA, APRIL 29-MAY 2, 1988. CLIN RES. (1988) 36 (3), 402A.
CODEN: CLREAS. ISSN: 0009-9279.

L16 ANSWER 59 OF 107 CAPLUS COPYRIGHT 2003 ACS
AU Song, Dexiu; Ni, Binhui; Dai, Zhonghan; Shi, Yinghsien
TI Molecular cloning of bovine growth hormone cDNA
SO Shengwu Gongcheng Xuebao (1988), 4(1), 20-5
CODEN: SGXUED; ISSN: 1000-3061

L16 ANSWER 60 OF 107 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AU MARSH L E; GUILFOYLE T J
TI CAULIFLOWER MOSAIC VIRUS REPLICATION INTERMEDIATES ARE ENCAPSIDATED INTO VIRION-LIKE PARTICLES.

SO VIROLOGY, (1987) 161 (1), 129-137.
CODEN: VIRLAX. ISSN: 0042-6822.

L16 ANSWER 61 OF 107 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AU MOSES D F; ORTI E; DE NICOLA A F
TI A COMPARISON OF THE GLUCOCORTICOID RECEPTOR SYSTEM IN THE SPINAL CORD AND HIPPOCAMPUS.
SO BRAIN RES, (1987) 408 (1-2), 118-124.
CODEN: BRREAP. ISSN: 0006-8993.

L16 ANSWER 62 OF 107 CAPLUS COPYRIGHT 2003 ACS
AU McPherson, Alexander; Brayer, Gary; Cascio, Duilio; Williams, Roger
TI The mechanism of binding of a polynucleotide chain to pancreatic ribonuclease
SO Science (Washington, DC, United States) (1986), 232(4751), 765-8
CODEN: SCIEAS; ISSN: 0036-8075

L16 ANSWER 63 OF 107 CAPLUS COPYRIGHT 2003 ACS
AU McPherson, Alexander; Koszelak, Stanley; Axelrod, Herbert; Day, John; Robinson, Lindsay; McGrath, Mary; Williams, Roger; Cascio, Duilio
TI The effects of neutral detergents on the crystallization of soluble proteins
SO Journal of Crystal Growth (1986), 76(3), 547-53
CODEN: JCRGAE; ISSN: 0022-0248

L16 ANSWER 64 OF 107 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AU PATEL R; KVACH J T; MOUNTS P
TI ISOLATION AND RESTRICTION ENDONUCLEASE ANALYSIS OF MYCOBACTERIAL DNA.
SO J GEN MICROBIOL, (1986) 132 (2), 541-552.
CODEN: JGMIAN. ISSN: 0022-1287.

L16 ANSWER 65 OF 107 CAPLUS COPYRIGHT 2003 ACS
AU Yuan, Chuanzhao; Wu, Yun; Zeng, Weiqiang; Xiao, Xengqian
TI High resolution NMR studies of RNase and PNPase and their interaction with substrates
SO Shengwu Huaxue Yu Shengwu Wuli Xuebao (1986), 18(5), 397-403
CODEN: SHWPAU; ISSN: 0582-9879

L16 ANSWER 66 OF 107 CAPLUS COPYRIGHT 2003 ACS
AU McPherson, Alexander; Brayer, Gary D.; Morrison, Robert D.
TI Crystal structure of RNase A complexed with d(pA)4
SO Journal of Molecular Biology (1986), 189(2), 305-27
CODEN: JMOBAK; ISSN: 0022-2836

L16 ANSWER 67 OF 107 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AU JARAMILLO S; LASTRA R
TI PURIFICATION AND PROPERTIES OF THE GEMINIVIRUS EUPHORBIA MOSAIC VIRUS.
SO J PHYTOPATHOL (BERL), (1986) 115 (3), 193-203.
CODEN: JPHYEB.

L16 ANSWER 68 OF 107 MEDLINE DUPLICATE 23
AU Wu G J; Cannon R E
TI An economical large scale procedure to purify E. coli amplifiable plasmids for DNA sequencing, in vitro transcription and in vitro mutagenesis.
SO EXPERIENTIA, (1985 Nov 15) 41 (11) 1488-90.
Journal code: 0376547. ISSN: 0014-4754.

L16 ANSWER 69 OF 107 MEDLINE DUPLICATE 24
AU Rossini G P
TI RNase A effects on sedimentation and DNA binding properties of dexamethasone-receptor complexes from HeLa cell cytosol.
SO JOURNAL OF STEROID BIOCHEMISTRY, (1985 Jan) 22 (1) 47-56.
Journal code: 0260125. ISSN: 0022-4731.

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L16 ANSWER 20 OF 107 MEDLINE DUPLICATE 5
AU Phoenix P; Raymond M A; Masse E; Drolet M
TI Roles of DNA topoisomerases in the regulation of R-loop formation in vitro.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Jan 17) 272 (3) 1473-9.
Journal code: 2985121R. ISSN: 0021-9258.

L16 ANSWER 21 OF 107 CAPLUS COPYRIGHT 2003 ACS
AU Strunk, Guenther; Ederhof, Tobias
TI Machines for automated evolution experiments in vitro based on the serial-transfer concept
SO Biophysical Chemistry (1997), 66(2-3), 193-202
CODEN: BICIAZ; ISSN: 0301-4622

L16 ANSWER 22 OF 107 MEDLINE DUPLICATE 6
AU Benore-Parsons M; Ayoub M A
TI Presence of **RNase A** causes aberrant **DNA** band shifts.
SO BIOTECHNIQUES, (1997 Jul) 23 (1) 128-31.
Journal code: 8306785. ISSN: 0736-6205.

L16 ANSWER 23 OF 107 MEDLINE DUPLICATE 7
AU Rubsam L Z; Shewach D S
TI Improved method to prepare RNA-free DNA from mammalian cells.
SO JOURNAL OF CHROMATOGRAPHY. B, BIOMEDICAL SCIENCES AND APPLICATIONS, (1997 Nov 21) 702 (1-2) 61-8.
Journal code: 9714109. ISSN: 1387-2273.

L16 ANSWER 24 OF 107 CAPLUS COPYRIGHT 2003 ACS
AU Rzhetsky, Andrey; Dopazo, Joaquin; Snyder, Eric; Dangler, Charles A.; Ayala, Francisco Jose
TI Assessing dissimilarity of genes by comparing their RNAse A mismatch cleavage patterns
SO Genetics (1996), 144(4), 1975-1983
CODEN: GENTAE; ISSN: 0016-6731

L16 ANSWER 25 OF 107 MEDLINE DUPLICATE 8
AU Pohjanpelto P; Holtta E
TI Phosphorylation of Okazaki-like DNA fragments in mammalian cells and role of polyamines in the processing of this DNA.
SO EMBO JOURNAL, (1996 Mar 1) 15 (5) 1193-200.
Journal code: 8208664. ISSN: 0261-4189.

L16 ANSWER 26 OF 107 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. DUPLICATE 9
AU Laitinen, Ann Marie (1); Otvos, Imre S.; Levin, David B. (1)
TI Geographic distribution of cytoplasmic polyhedrosis virus infection in Douglas-fir tussock moth larvae, Orgyia pseudotsugata, in British Columbia.
SO Journal of Invertebrate Pathology, (1996) Vol. 67, No. 3, pp. 229-235.
ISSN: 0022-2011.

L16 ANSWER 27 OF 107 CAPLUS COPYRIGHT 2003 ACS
AU Ozeki, Kenji; Hizume, Kazuhisa; Kanda, Akihiro; Hamachi, Masaaki; Nunokawa, Yataro
TI A method for the re-isolation of an autonomously replicating plasmid from Aspergillus transformants
SO Bioscience, Biotechnology, and Biochemistry (1995), 59(6), 1133-4
CODEN: BBBIEJ; ISSN: 0916-8451

L16 ANSWER 28 OF 107 CAPLUS COPYRIGHT 2003 ACS

AU Elstein, Kenneth H.; Thomas, David J.; Zucker, Robert M.
TI Factors affecting flow cytometric detection of apoptotic nuclei by DNA analysis
SO Cytometry (1995), 21(2), 170-6
CODEN: CYTODQ; ISSN: 0196-4763

L16 ANSWER 29 OF 107 CAPLUS COPYRIGHT 2003 ACS
AU Meller, Victoria H.; McConnell, Maeve; Fisher, Paul A.
TI An RNase-sensitive particle containing Drosophila melanogaster DNA topoisomerase II
SO Journal of Cell Biology (1994), 126(6), 1331-40
CODEN: JCLBA3; ISSN: 0021-9525

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     (FILE 'HOME' ENTERED AT 18:25:02 ON 14 JAN 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 18:25:23 ON 14 JAN
     2003
L1             8 S HIV(5A)PACKAGING(W)SITE
L2           447 S HIV(5A)PACKAGING
L3        432474 S SPLICE(W)DONOR OR SD
L4         62852 S SPLICE(W)ACCEPTOR OR SA
L5           484 S HIV(6A)REV(4A)BIND?
L6             0 S L2 AND L3 AND L4 AND L5
L7             1 S L2 AND L3 AND L4
L8         10670 S EDN OR EOSINOPHIL-DERIV?(3A)NEUROTOXIN OR RNASE(W)A
L9           388 S (NUCLEIC(W)ACID OR POLYNUCLEOTIDE OR DNA)(8A)L8
L10          261 S (NUCLEIC(W)ACID OR POLYNUCLEOTIDE OR DNA)(5A)L8
L11          219 S (SUPPRESS? OR INHIBIT? OR DIMINISH? OR DECREAS?)(6A)REPLICATI
L12            0 S L10(S)L11
L13            0 S L10 AND L11
L14          161 DUP REM L10 (100 DUPLICATES REMOVED)
L15          166 S (NUCLEIC(W)ACID OR POLYNUCLEOTIDE OR DNA)(3A)L8
L16          107 DUP REM L15 (59 DUPLICATES REMOVED)
L17         1387 S EDN
L18       156977 S ANTIVIRAL
L19           36 S L17 AND L18
L20           14 DUP REM L19 (22 DUPLICATES REMOVED)

=> d au ti so ab 1-14 l20

L20  ANSWER 1 OF 14  CAPLUS  COPYRIGHT 2003 ACS        DUPLICATE 1
AU   Zhang, Jianzhi; Rosenberg, Helene F.
TI   Complementary advantageous substitutions in the evolution of an
     antiviral RNase of higher primates
SO   Proceedings of the National Academy of Sciences of the United States of
     America (2002), 99(8), 5486-5491
     CODEN: PNASA6; ISSN: 0027-8424
AB   An improved understanding of the evolution of gene function at the mol.
     level may provide significant insights into the origin of biol. novelty
     and adaptation.  With the approach of ancestral protein reconstruction, we
     here address the question of how a dramatically enhanced ribonucleolytic
     activity and the related antiviral activity evolved in a
     recently duplicated RNase (eosinophil-derived neurotoxin) gene of higher
     primates.  We show that the mother gene of the duplicated genes had
     already possessed a weak antiviral activity before duplication.
     After duplication, substitutions at two interacting sites
     (Arg-64.fwdarw.Ser and Thr-132.fwdarw.Arg) resulted in a 13-fold
     enhancement of the ribonucleolytic activity of eosinophil-derived
     neurotoxin.  These substitutions are also necessary for the potent
     antiviral activity, with contributions from addnl. amino acid
     changes at interacting sites.  Our observation that a change in
     eosinophil-derived neurotoxin function occurs only when both interacting
     sites are altered indicates the importance of complementary substitutions
     in protein evolution.  Thus, neutral substitutions are not simply "noises"
     in protein evolution, as many have thought.  They may play constructive
     roles by setting the intramol. microenvironment for further complementary
     advantageous substitutions, which can lead to improved or altered
     function.  Overall, our study illustrates the power of the "paleomol.
     biochem." approach in delineating the complex interplays of amino acid
     substitutions in evolution and in identifying the mol. basis of biol.
     innovation.

L20  ANSWER 2 OF 14      MEDLINE                          DUPLICATE 2
AU   Swaminathan G Jawahar; Holloway Daniel E; Veluraja Kasinadar; Acharya K
     Ravi
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TI Atomic resolution (0.98 A) structure of eosinophil-derived neurotoxin.
SO BIOCHEMISTRY, (2002 Mar 12) 41 (10) 3341-52.
Journal code: 0370623. ISSN: 0006-2960.
AB Human eosinophil-derived neurotoxin (**EDN**) is a small, basic protein that belongs to the ribonuclease A superfamily. **EDN** displays **antiviral** activity and causes the neurotoxic Gordon phenomenon when injected into rabbits. Although **EDN** and ribonuclease A have appreciable structural similarity and a conserved catalytic triad, their peripheral substrate-binding sites are not conserved. The crystal structure of recombinant **EDN** (rEDN) has been determined at 0.98 A resolution from data collected at a low temperature (100 K). We have refined the crystallographic model of the structure using anisotropic displacement parameters to a conventional R-factor of 0.116. This represents the highest resolution structure of rEDN determined to date and is only the second ribonuclease structure to be determined at a resolution greater than 1.0 A. The structure provides a detailed picture of the conformational freedom at the various subsites of rEDN, and the water structure accounts for more than 50% of the total solvent content of the unit cell. This information will be crucial for the design of tight-binding inhibitors to restrain the ribonucleolytic activity of rEDN.

L20 ANSWER 3 OF 14 MEDLINE DUPLICATE 3
AU Leonidas D D; Boix E; Prill R; Suzuki M; Turton R; Minson K; Swaminathan G J; Youle R J; Acharya K R
TI Mapping the ribonucleolytic active site of eosinophil-derived neurotoxin (**EDN**). High resolution crystal structures of **EDN** complexes with adenylic nucleotide inhibitors.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 May 4) 276 (18) 15009-17.
Journal code: 2985121R. ISSN: 0021-9258.
AB Eosinophil-derived neurotoxin (**EDN**), a basic ribonuclease found in the large specific granules of eosinophils, belongs to the pancreatic RNase A family. Although its physiological function is still unclear, it has been shown that **EDN** is a neurotoxin capable of inducing the Gordon phenomenon in rabbits. **EDN** is also a potent helminthotoxin and can mediate **antiviral** activity of eosinophils against isolated virions of the respiratory syncytial virus. **EDN** is a catalytically efficient RNase sharing similar substrate specificity with pancreatic RNase A with its ribonucleolytic activity being absolutely essential for its neurotoxic, helminthotoxic, and **antiviral** activities. The crystal structure of recombinant human **EDN** in the unliganded form has been determined previously (Mosimann, S. C., Newton, D. L., Youle, R. J., and James, M. N. G. (1996) J. Mol. Biol. 260, 540-552). We have now determined high resolution (1.8 A) crystal structures for **EDN** in complex with adenosine-3',5'-diphosphate (3',5'-ADP), adenosine-2',5'-di-phosphate (2',5'-ADP), adenosine-5'-diphosphate (5'-ADP) as well as for a native structure in the presence of sulfate refined at 1.6 A. The inhibition constant of these mononucleotides for **EDN** has been determined. The structures present the first detailed picture of differences between **EDN** and RNase A in substrate recognition at the ribonucleolytic active site. They also provide a starting point for the design of tight-binding inhibitors, which may be used to restrain the RNase activity of **EDN**.

L20 ANSWER 4 OF 14 MEDLINE DUPLICATE 4
AU Rosenberg H F; Domachowske J B
TI Eosinophils, eosinophil ribonucleases, and their role in host defense against respiratory virus pathogens.
SO JOURNAL OF LEUKOCYTE BIOLOGY, (2001 Nov) 70 (5) 691-8. Ref: 63
Journal code: 8405628. ISSN: 0741-5400.
AB Eosinophils remain among the most enigmatic of cells, as our appreciation of their detrimental activities--e.g., asthma and allergic disease--far outweighs our understanding of their beneficial effects. Among the major

secretory effector proteins of eosinophils are the ribonucleases eosinophil-derived neurotoxin (**EDN**) and eosinophil cationic protein (ECP) in primates and their orthologs, the eosinophil-associated ribonucleases (EARs) in rodents. The rapid diversification observed among these ribonucleases suggested that the ultimate target(s) might be similarly efficient at generating sequence diversity while maintaining an unalterable susceptibility to ribonucleolytic cleavage. This has prompted us to consider a role for these proteins and by extension, for eosinophils, in host defense against single-stranded RNA virus pathogens. We detail our studies of the **antiviral** activity of eosinophils and eosinophil ribonucleases against respiratory syncytial virus (RSV) in vitro and the related, natural rodent pathogen, pneumonia virus of mice (PVM), in vivo, and consider the possibility that **antiviral** host defense and the dysregulated responses leading to asthma represent opposing sides of an eosinophil-mediated double-edged sword.

L20 ANSWER 5 OF 14 SCISEARCH COPYRIGHT 2003 ISI (R)
AU Nakajima M; Hirakata M; Nittoh T; Ishihara K; Ohuchi K (Reprint)
TI Expression and purification of recombinant rat eosinophil-associated ribonucleases, homologues of human eosinophil cationic protein and eosinophil-derived neurotoxin, and their characterization
SO INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (JUL 2001) Vol. 125, No. 3, pp. 241-249.
Publisher: KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND.
ISSN: 1018-2438.
AB Background. Human eosinophils contain two eosinophil ribonucleases, eosinophil cationic protein (ECP) and eosinophil-derived neurotoxin (**EDN**). In rats, 8 homologues of human ECP and **EDN** have been identified. To clarify the biological activity of rat eosinophil ribonucleases, we cloned rat eosinophil-associated ribonuclease (EAR)-1/rat ribonuclease 7 and rat EAR-2/rat ribonuclease 4, and produced recombinant rat pre-EAR-1 and pre-EAR-2 in a bacterial expression system. Methods:As we have already cloned the complete nucleotide sequence for rat EAR-1, we determined that for rat EAR-2 cDNA by the rapid amplification of cDNA ends procedure. Recombinant rat pre-EAR-1 and pre-EAR-2 were expressed in Escherichia coli as N-terminal 6 x histidine tagged proteins, isolated from the insoluble fraction of the cell lysate and purified by a single-step method using an Ni-NTA resin column after solubilization with a 6 M guanidine solution. Results: The deduced amino acid sequence revealed that the molecular weight of EAR-2 containing the signal peptide is 17.3 kD and the isoelectric point is 8.59. The homology in amino acid sequence between rat pre-EAR-2, and human pre-ECP and human pre-**EDN** is 51 and 53%, respectively. The purified and refolded recombinant rat pre-EAR-1 and pre-EAR-2 showed bactericidal activity against E. coli and Staphylococcus aureus. Conclusions: These findings suggest that rat EAR-1 and EAR-2 act as host defense factors against bacterial infection in rats. Copyright (C) 2001 S. Karger AG, Basel.

L20 ANSWER 6 OF 14 SCISEARCH COPYRIGHT 2003 ISI (R)
AU Zhang J; Rosenberg H F (Reprint)
TI Sequence variation at two eosinophil-associated ribonuclease loci in humans
SO GENETICS, (DEC 2000) Vol. 156, No. 4, pp. 1949-1958.
Publisher: GENETICS, 428 EAST PRESTON ST, BALTIMORE, MD 21202.
ISSN: 0016-6731.
AB Host defense against invading pathogens is of great importance to the survival of higher organisms. We hale been studying the evolution of mammalian eosinophil-associated ribonucleases (EARs), which ar-e members of the ribonuclease A super-family with known antipathogen activities. Earlier studies showed that positive: selection promoted rapid diversification of paralogous EAR. genes in both primates and rodents. Intraspecifically, however, it is unknown whether these genes also have divergent alleles. The recent discovery that the gene repertoire of the EAR family is much larger in rodents than in primates has led us to

consider the possibility that primates maintain a large number of polymorphic alleles to compensate for a smaller gene repertoire. Here we present sequences of 2417 nucleotides at the two EAR loci, the eosinophil-derived neurotoxin (**EDN**, RNase 2) and eosinophil cationic protein (ECP, RNase 3), from >50 human individuals. Our data demonstrate dial the nucleotide diversities (0.06-0.11%) at these loci are typical for human nuclear genes, thus permitting us to reject this polymorphism hypothesis. No significant departure from neutrality is noted and no signs of overdominant selection are observed. Similar patterns were observed in a preliminary study of chimpanzees. In summary, our results suggest that the antipathogen functions of the primate EARs are conserved after they are established and that these proteins are not currently undergoing rapid diversification in response to challenge from invading microorganisms.

L20 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2003 ACS
IN Rosenberg, Helene F.; Domachowske, Joseph B.
TI Eosinophil-derived RNases for inactivating enveloped RNA virus particles and therapy of viral infections
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
AB Disclosed is a method for inactivating a virion of an enveloped RNA virus comprising contacting the virion with an eosinophil-derived RNase, such as eosinophil-derived neurotoxin (**EDN**) or eosinophil cationic protein (ECP). The invention also provides methods for treating a subject infected by an enveloped RNA virus and for preventing infection by an enveloped RNA virus comprising administering an effective amt. of an eosinophil-derived RNase, such as **EDN** or ECP. The invention also provides a compn. comprising an effective amt. of an eosinophil-derived RNase and an acceptable carrier.

L20 ANSWER 8 OF 14 MEDLINE DUPLICATE 5
AU Singhania N A; Dyer K D; Zhang J; Deming M S; Bonville C A; Domachowske J B; Rosenberg H F
TI Rapid evolution of the ribonuclease A superfamily: adaptive expansion of independent gene clusters in rats and mice.
SO JOURNAL OF MOLECULAR EVOLUTION, (1999 Dec) 49 (6) 721-8.
Journal code: 0360051. ISSN: 0022-2844.
AB The two eosinophil ribonucleases, eosinophil-derived neurotoxin (**EDN**/RNase 2) and eosinophil cationic protein (ECP/RNase 3), are among the most rapidly evolving coding sequences known among primates. The eight mouse genes identified as orthologs of **EDN** and ECP form a highly divergent, species-limited cluster. We present here the rat ribonuclease cluster, a group of eight distinct ribonuclease A superfamily genes that are more closely related to one another than they are to their murine counterparts. The existence of independent gene clusters suggests that numerous duplications and diversification events have occurred at these loci recently, sometime after the divergence of these two rodent species (approximately 10-15 million years ago). Nonsynonymous substitutions per site (d(N)) calculated for the 64 mouse/rat gene pairs indicate that these ribonucleases are incorporating nonsilent mutations at accelerated rates, and comparisons of nonsynonymous to synonymous substitution (d(N) / d(S)) suggest that diversity in the mouse ribonuclease cluster is promoted by positive (Darwinian) selection. Although the pressures promoting similar but clearly independent styles of rapid diversification among these primate and rodent genes remain uncertain, our recent findings regarding the function of human **EDN** suggest a role for these ribonucleases in **antiviral** host defense.

L20 ANSWER 9 OF 14 MEDLINE DUPLICATE 6
AU Rosenberg H F; Domachowske J B
TI Eosinophils, ribonucleases and host defense: solving the puzzle.
SO IMMUNOLOGIC RESEARCH, (1999) 20 (3) 261-74. Ref: 66

Journal code: 8611087. ISSN: 0257-277X.

AB The eosinophil ribonucleases eosinophil-derived neurotoxin (**EDN** /RNase 2) and eosinophil cationic protein (ECP/RNase 3) are among the major secretory effector proteins of human eosinophilic leukocytes, cells whose role in host defense remains controversial and poorly understood. We have recently described the unusual manner in which this ribonuclease lineage has evolved, with extraordinary diversification observed in primate as well as in rodent **EDNs** and ECPs. The results of our evolutionary studies suggest that the **EDN**/ ECP ribonucleases are in the process of being tailored for a specific, ribonuclease-related goal. With this in mind, we have begun to look carefully at some of the intriguing associations that link eosinophils and their ribonucleases to disease caused by the single-stranded RNA viral pathogen, respiratory syncytial virus (RSV). Recent work in our laboratory has demonstrated that eosinophils can mediate a direct, ribonuclease-dependent reduction in infectivity of RSV in vitro, and that **EDN** can function alone as an independent **antiviral** agent. The results of this work have led us to consider the possibility that the **EDN**/ECP ribonucleases represent a heretofore unrecognized element of innate and specific **antiviral** host defense.

L20 ANSWER 10 OF 14 MEDLINE

AU Kauffman H F; Hovenga H; de Bruijn H W; Beintema J J

TI Eosinophil derived neurotoxin (**EDN**) levels in commercial human urinary preparations of glycoprotein hormones.

SO EUROPEAN JOURNAL OF OBSTETRICS, GYNECOLOGY, AND REPRODUCTIVE BIOLOGY, (1999 Jan) 82 (1) 111-3.
Journal code: 0375672. ISSN: 0301-2115.

AB Eosinophil derived neurotoxin (**EDN**) is a ubiquitous human ribonuclease, occurring not only in eosinophils, but also in many tissues and body fluids. It may be a contaminant of commercial human urinary preparations of chorionic gonadotropin (hCG) and other glycoprotein hormones. Here we describe the use of a fast commercial assay to quantify this contaminant and demonstrate that the content varies much between different commercial glycoprotein hormone preparations. As this ribonuclease may have a cytotoxic activity on certain cells, it is useful to be able to determine its quantity in a fast and reliable way in these preparations.

L20 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2003 ACS

IN Raybak, Susanna M.; Cara, Andrea; Gusella, Gabriele Luca; Newton, Dianne L.

TI Construction of retroviral vectors for delivering viral and oncogenic inhibitors

SO PCT Int. Appl., 63 pp.
CODEN: PIXXD2

AB Cell transformation vectors for inhibiting HIV and tumor growth are provided. Optionally, the vectors encode RNAses A superfamily members such as eosinophil-derived neurotoxin (**EDN**) and onconase. Cells transduced by the vectors and methods of transforming cells (in vitro and in vivo) using the vectors are also provided. The viral and oncogene inhibitors are typically linked to a promoter such as retroviral HIV LTR promoters, the CMV promoter, the probasin promoter, and tetracycline-responsive promoters. The method is exemplified by construction of a viral vector contg. a HIV Rev-responsive element, an encephalomycocarditis virus internal ribosome entry site, a first viral inhibitor subsequence (for immunodominant proteins such as as Tat, Gag, or Rev), splice donor site subsequence, splice acceptor site subsequence, the above mentioned promoter, and the **EDN** coding sequence. The vector may be packaged in a liposome and its contents transduced into CD34+ hematopoietic stem cells, CD4+ cells, and transferrin receptor+ cells. Claimed vectors include pBAR, pBAR-ONC, and pBAR-**EDN**.

L20 ANSWER 12 OF 14 MEDLINE DUPLICATE 7

AU Domachowske J B; Bonville C A; Dyer K D; Rosenberg H F
TI Evolution of **antiviral** activity in the ribonuclease A gene superfamily: evidence for a specific interaction between eosinophil-derived neurotoxin (**EDN**/RNase 2) and respiratory syncytial virus.
SO NUCLEIC ACIDS RESEARCH, (1998 Dec 1) 26 (23) 5327-32.
Journal code: 0411011. ISSN: 0305-1048.
AB We have demonstrated that the human eosinophil-derived neurotoxin (**EDN**, RNase 2), a rapidly evolving secretory protein derived from eosinophilic leukocytes, mediates the ribonucleolytic destruction of extracellular virions of the single-stranded RNA virus respiratory syncytial virus (RSV). While RNase activity is crucial to **antiviral** activity, it is clearly not sufficient, as our results suggest that **EDN** has unique structural features apart from RNase activity that are necessary to promote **antiviral** activity. We demonstrate here that the interaction between **EDN** and extracellular virions of RSV is both saturatable and specific. Increasing concentrations of the antivirally inactivated, ribonucleolytically inactivated point mutant form of recombinant human **EDN**, rhEDNdK38, inhibits rhEDN's **antiviral** activity, while increasing concentrations of the related RNase, recombinant human RNase k6, have no effect whatsoever. Interestingly, acquisition of **antiviral** activity parallels the evolutionary development of the primate **EDN** lineage, having emerged some time after the divergence of the Old World from the New World monkeys. Using this information, we created ribonucleolytically active chimeras of human and New World monkey orthologs of **EDN** and, by evaluating their **antiviral** activity, we have identified an N-terminal segment of human **EDN** that contains one or more of the sequence elements that mediate its specific interaction with RSV.

L20 ANSWER 13 OF 14 MEDLINE DUPLICATE 8
AU Domachowske J B; Dyer K D; Adams A G; Leto T L; Rosenberg H F
TI Eosinophil cationic protein/RNase 3 is another RNase A-family ribonuclease with direct **antiviral** activity.
SO NUCLEIC ACIDS RESEARCH, (1998 Jul 15) 26 (14) 3358-63.
Journal code: 0411011. ISSN: 0305-1048.
AB Eosinophil cationic protein (ECP) is one of two RNase A-superfamily ribonucleases found in secretory granules of human eosinophilic leukocytes. Although the physiologic function of eosinophils [and thus of the two eosinophil ribonucleases, ECP and eosinophil-derived neurotoxin (**EDN**)] remains controversial, we have recently shown that isolated human eosinophils promote ribonuclease-dependent toxicity toward extracellular virions of the single-stranded RNA virus, respiratory syncytial virus, group B (RSV-B). We have also shown that recombinant human **EDN** (rhEDN) can act alone as a ribonuclease-dependent **antiviral** agent. In this work, we provide a biochemical characterization of recombinant human ECP (rhECP) prepared in baculovirus, and demonstrate that rhECP also promotes ribonuclease-dependent **antiviral** activity. The rhECP described here is N-glycosylated, as is native ECP, and has approximately 100-fold more ribonuclease activity than non-glycosylated rhECP prepared in bacteria. The enzymatic activity of rhECP was sensitive to inhibition by placental ribonuclease inhibitor (RI). Although rhECP was not as effective as rhEDN at reducing viral infectivity (500 nM rhECP reduced infectivity of RSV-B approximately 6 fold; 500 nM rhEDN, >50 fold), the **antiviral** activity appears to be unique to the eosinophil ribonucleases; no reduction in infectivity was promoted by bovine RNase A, by the amphibian ribonuclease, onconase, nor by the closely-related human ribonuclease, RNase k6. Interestingly, combinations of rhEDN and rhECP did not result in either a synergistic or even an additive **antiviral** effect. Taken together, these results suggest that that the interaction between the eosinophil ribonucleases and the extracellular virions of RSV-B may be specific and saturable.

L20 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2003 ACS

AU Cara, A.; Rybak, S. M.; Newton, D. L.; Crowley, R.; Rottschafer, S. E.; Reitz, M. S., Jr.; Gusella, G. L.

TI Inhibition of HIV-1 replication by combined expression of gag dominant negative mutant of a human ribonuclease in a tightly controlled HIV-1 inducible vector

SO Gene Therapy (1998), 5(1), 65-75
CODEN: GETHEC; ISSN: 0969-7128

AB An HIV-1-based expression vector has been constructed that produces protective genes tightly regulated by HIV-1 Tat and Rev proteins. The vector contains either a single protective gene (HIV-1 gag dominant neg. mutant (delta-gag)) or a combination of two different protective genes (delta-gag and eosinophil-derived neurotoxin (**EDN**), a human RNase) which are expressed from a dicistronic mRNA. After stable transfection of CEM T cells and following challenge with HIV-1, viral prodn. was completely inhibited in cells transduced with the vector producing both delta-gag and **EDN** and delayed in cells producing delta-gag alone. In addn., cotransfection of HeLa-Tat cells with an infectious HIV-1 mol. clone and either protective vector demonstrated that the HIV-1 packaging signals present in the constructs were functional and allowed the efficient assembly of the protective RNAs into HIV-1 virions, thus potentially transmitting protection to the HIV-1 target cells.

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